REMARKS/ARGUMENTS

1. Request of Proper Alignment of Drawings

The instant patent application was published on February 7, 2002 with Publication No. 2002/0016636. The drawings, particularly the drawing on the cover page, were not properly aligned. Applicants respectfully request appropriate alignment and centering of all drawings of the instant patent application at the time of issuing.

2. Remarks on the Amendment

Claims 1, 7-10, 12, 14-18, 21-24, 26, 29-32, 36 and 41 have been amended to more specifically define Applicants' claimed invention. Claims 6 and 18 have been canceled. New claims 42-71 have been added. Antecedent basis of the new claims can be found in the Specification and claims as filed, more specifically on page 8, line 19 to page 9, line 10, and Claims 10 and 24. Applicants respectfully submit that no new matter has been added by the amendments and the new claims.

After cancellation of two claims, and addition of 30 claims, there are now total of 69 claims pending. Applicants submit an additional fee in amount of $336.00 for 2 extra independent claims and 28 extra claims. As stated previously, please charge the Deposit Account No. 502,557.

3. Response to the rejection of Claims 15, 16, 17, 29, 30, 32 and 41 based upon 35 USC §112

Claims 15, 16, 17, 29, 30, 32 and 41 stand rejected under 35 USC 112, second paragraph. This rejection is respectfully traversed by the amendments.

Applicants have amended Claims 15, 16, 17, 29, 30, 32 and 41 to more

specifically define Applicants' claimed invention.

The Examiner states that the recited "derivatives" in Claims 15 and 29 is indefinite in not specifying particular substitutes or functional groups. Applicant respectfully point out that poly(desaminotyrosyl-tyrosine ethyl ester carbonates), abbreviated as poly(DTE carbonate), is a polycarbonate of desaminotyrosyl-tyrosine alkyl ester, which has a molecular structure as shown below:

$$-[O\text{-}C_6H_6\text{-}CH_2\text{-}CH_2\text{-}CO\text{-}NH\text{-}CH(COOY)\text{-}CH_2\text{-}C_6H_6\text{-}COO\text{-}]_n-$$

where Y = ethyl.

It is known to those skilled in the art that the derivates of poly(desaminotyrosyl-tyrosine ethyl ester carbonates) include a group of polycarbonates of desaminotyrosyl-tyrosine alkyl esters with varying chain length of the alkyl ester pendent chain. More specifically, following poly(DTE carbonate) derivatives have been used as biomaterials in research and applications:

Y = butyl, poly(DTB carbonate)

Y = hexyl, poly(DTH carbonate)

Y = octyl, poly(DTO carbonate)

Applicants submit herein Abstracts of four articles related to poly(DTE carbonate) and derivatives. Since the polycarbonates of desaminotyrosyl-tyrosine alkyl esters were known to those skilled in the art at the time of the invention was made, Applicants believe that Applicants' claimed poly(desaminotyrosyl-tyrosine ethyl ester carbonates) and derivatives are clearly understood by those skilled in the art, therefore, are not indefinite.

Accordingly, Applicants respectfully request withdrawal of the rejection of Claims based upon 35 U.S.C. §112, second paragraph.

4. Response to the Objection of Claims 6-14, 15-17, 20-28, 29, 30, 31, 32 and 41

Claims 6-14, 15-17, 20-28, 29, 30, 31, 32 and 41 are objected to as being

dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims. Applicants thank for the Examiner for indicating the allowability of these claims. This objection is obviated by amendments.

The original Claims 7-14 and 15-17 are dependent claims of Claim 6 which is a dependent claim of Claim 1. Similarly, the original Claims 21-28, 29, 30 and 31 are dependent claims of Claim 20 which is a dependent claim of Claim 18. Applicants have amended Claim 1 by incorporating all claim limitations of original Claim 6, and have amended Claim 18 by incorporating all claim limitations of original Claim 20. These amendments are equivalent to rewrite Claims 6 and 20 in independent form as suggested by the Examiner.

More specifically, the claim scope of amended Claim 1 is the same to that of original Claim 6, and the claim scope of amended Claim 18 is the same to that of original Claim 20, respectively. The original Claims 6 and 20 have been canceled because they become redundant after the amendment of Claims 1 and 18. Claims 7-14 and 15-17 are dependent claims of amended Claim 1, and Claims 21-28, 29, 30, 31, and 32 are dependent claims of amended Claim 18, therefore, are in condition for allowance.

Claim 41 is a dependent claim of Claim 36 which has been amended, see response related to Claim 36 hereinafter. Applicants believe that amended Claim 36 and its dependent claims are in condition for allowance.

Accordingly, Applicants respectfully request allowance of Claims 6-14, 15-17, 20-28, 29, 30, 31, 32 and 41.

5. Response to the Rejections of Claims 1, 4, 5, 18 and 19 Based Upon 35 USC §102(e)

Claims 1, 4, 5, 18 and 19 stand rejected under 35 U.S.C. §102(e) as being anticipated by Petersen (US 2002/0110541). This rejection is respectfully traversed by the amendments.

The status of Claims 1, 4, 5, 18 and 19 has been addressed above. The amended Claims 1 and 18 which have incorporated all claim limitations of the original claims 6 and 20 respectively, and their dependent claims 4, 5 and 19 are allowable as suggested by the Examiner.

Accordingly, Applicant respectfully requests withdrawal of the rejection of Claims 1, 4, 5, 18 and 19 based upon 35 U.S.C. §102(e).

6. Response to the Rejections of Claims 1, 4, 5, 18, 19, 33-37, 39 and 40 Based Upon 35 USC §102(e) or §103(a)

Claims 1, 4, 5, 18, 19, 33-37, 39 and 40 stand rejected under 35 U.S.C. §102(e), as being anticipated by, or alternatively under §103(a) as obvious over Petersen (US 2002/0110541). This rejection is respectfully traversed.

The status of Claims 1 and 18 has been addressed above. Claims 4 and 5 are dependent claims of amended Claim 1, and Claims 19 and 33-35 are dependent claims of amended Claim 18, respectively, therefore, are in condition for allowance.

This response only addresses Claims 36, 37, 39 and 40. Claim 36 is an independent claim and Claim 37, 39 and 40 are dependent claims of Claim 36. Applicants' claimed invention defined by Claim 36 is a method for bone augmentation and bone defect reparation which comprises the steps of mixing a calcium sulfate compound and resorbable polymer coated particles with a setting agent into a mixture; applying said mixture; and setting said mixture into a heterogeneous solid composition, wherein upon setting, said calcium sulfate compound forms a matrix and said resorbable polymer coated particles settled within said matrix; and wherein said heterogeneous solid composition resorbs at a controlled rate in a recipient site for stimulating bone growth.

Petersen teaches a bone graft substitute composition which includes calcium sulfate, a mixing solution, and a plasticizing substance comprising a cellulose derivative. Petersen further teaches the method for mixing the bone

graft substitute composition comprises the steps of (1) dry blend the powder components (i.e., calcium sulfate hemihydrate, carboxymethylcellulose, and demineralized bone matrix), (2) add the sterile water, and (3) mix or stir all components for approximately 30 seconds to one minute or until the desired putty-like consistency is achieved (paragraphs 0021, 0027, 0032 and 0036).

Petersen fails to teach Applicants' claimed method of using resorbable polymer coated particles for bone augmentation and bone defect reparation. Pertersen further fails to teach Applicants' claimed method which forms a matrix of a calcium sulfate compound and has resorbable polymer coated particles settled within said matrix. Moreover, Petersen fails to teach Applicants' claimed method which produces a heterogeneous solid composition that resorbs at a controlled rate in a recipient site for stimulating bone growth.

It is apparent that Applicants' essential step of mixing resorbable polymer coated particles, the key components of the composition, and resulting controlled rate of resorption are completely absent in Petersen's reference.

Therefore, Applicants' claimed method for bone augmentation and bone defect reparation is not anticipated or even implied by Petersen's teaching.

Furthermore, Petersen specifically teaches that his resultant bone graft substitute composition has the characteristics of handability, ejectability, and robustness. Based on Peterson's teaching one skilled in the art would not be motivated to try to use to his composition to obtain controlled rate of resorption in a recipient site. Even if one tried, one would not obtain Applicants' claimed method of using a calcium sulfate matrix with resorbable polymer coated particles settled within to achieve a controlled resorption rate. Therefore, Applicants maintain that the claimed invention defined by Claims 36, 37, 39 and 40 are unobvious in view of the prior art.

Accordingly, Applicant respectfully requests withdrawal of the rejection of Claims 1, 4, 5, 18, 19, 33-37, 39 and 40 based upon 35 U.S.C. §102(e) and §103(a).

7. Response to the Rejections of Claims 1-5 based upon 35 USC §103(a)

Claims 1-5 stand rejected under 35 U.S.C. §103(a) as being unpatentable over Norton et al (US 5,681,873) alone, or in view of Ricci et al (US 6,224,635), Gerhart et al (US 5,085,861) or Petersen (US 2002/0110541). This rejection is respectfully traversed by the amendments.

The status of Claim 1 has been addressed above. Claims 2-5 are dependent claims of amended Claim 1, therefore, are in condition for allowance.

Accordingly, Applicant respectfully requests withdrawal of the rejection of Claims 1-5 based upon 35 U.S.C. §103(a).

8. Response to the Rejections of Claims 1-5, 18, 19, 33-36 and 38-40 based upon 35 USC §103(a)

Claims 1-5, 18, 19, 33-36 and 38-40 stand rejected under 35 U.S.C. §103(a) as being unpatentable over Coopper et al (US 5,747,390) alone, or in view of Ricci et al (US 6,224,635), Gerhart et al (US 5,085,861) or Petersen (US 2002/0110541). This rejection is respectfully traversed.

The status of Claims 1 and 18 has been addressed above. Claims 2-5 are dependent claims of amended Claim 1, and Claims 19 and 33-35 are dependent claims of amended Claim 18, respectively, are therefore in condition for allowance.

This response only addresses Claims 36 and 38-40. Applicants' claimed invention defined by Claim 36 has been discussed above.

Coopper et al teach a biocompatible coated substrate which comprises (a) an absorbable substrate selected from the group consisting of woven meshes, nonwoven meshes, knitted meshes, yarns and fibers; and (b) a coating comprising a resorbable hard tissue osteo-conductive calcium containing powdered compound including calcium sulfate (Claims 1 and 2 of the reference).

Coopper et al fail to teach Applicants' claimed method of using resorbable

polymer coated particles for bone augmentation and bone defect reparation. Coopper et al further fail to teach Applicants' claimed method which forms a matrix of a calcium sulfate compound and has resorbable polymer coated particles settled within said matrix. Moreover, Coopper et al fail to teach Applicants' claimed method which produces a heterogeneous solid composition that resorbs at a controlled rate in a recipient site for stimulating bone growth.

It is well known to those skilled in the art that the current calcium sulfate based bone augmentation methods have deficiencies associated with rapid resorption rate of calcium sulfate compound. Applicants specifically described such problems in the Specification of the instant application, as recited below:

> When calcium sulfate is used as a cement to fill a bone void, fracture, or other defect, this material dissolves at a rapid rate, i.e., approximately one millimeter per week from the exterior of the cement towards the center thereof. Research of the present inventors has shown that this material causes precipitation of calcium phosphate deposits as it is resorbed at the surgical site. These precipitates, it has been shown, stimulate and direct the formation of new bone. ..... However, currently used calcium sulfate materials are resorbed by human bone within two to seven weeks, depending upon the calcium sulfate form and the particular surgical site, which cannot be retained at the site for longer periods. As noted, such material is resorbed faster than it can be replaced by new bone thereby reducing its value to both patient and practitioner.
>
> As such, the principal concern and difficulty expressed by practitioners (such as orthopedics or maxiofacial surgeons) are that calcium sulfate materials bio-resorb or dissolve too rapidly at a surgical or a recipient site, and, thereby, outpace the formation of new bone in human patients.

Applicants' claimed invention provides a method of using an improved implant composition to overcome the problems associated with rapid resorption rate of calcium sulfate compound. More specifically, Applicants' method of using a calcium sulfate matrix with resorbable polymer coated particles substantially extends the time of resorption of the implant composition, enabling a substantial match with the rate of new bone growth.

On the contrary, Cooper et al teach using calcium sulfate to coat a polymeric absorbable substrate. The reference does not address the rapid resorption rate of calcium sulfate compounds, instead, it teaches away from the Applicants' claimed invention by using calcium sulfate as the exterior coating.

Ricci et al, Gerhart et al, or Petersen does not correct the deficiencies of the primary reference described above.

Ricci et al teach a method of implanting an implant within the body of a patient which uses a wet surgical cement comprised of a calcium sulfate compound.

Gerhart et al teach a method of repairing living bone by applying a biodegradable bone cement which comprises a polymer matrix formed by cross-linking a biodegradable polyester of a dicarboxylic acid.

Petersen's teaching has been discussed above.

None of the three references teaches Applicants' claimed method of using resorbable polymer coated particles together with a calcium sulfate matrix to achieve a controlled rate of resorption of an implant composition. Similar to the primary reference, none of these three references addresses the deficiencies associated with the rapid resorption rate of calcium sulfate compounds.

One skilled in the art would not be motivated to try to achieve a controlled resorption rate of an implant composition by substituting Cooper et al's calcium sulfate coated polymeric substrates with Ricci et al, Gerhart et al, or Petersen's calcium sulfate hemihydrate. Even if one would combine the references' teaching, one would not obtain Applicants' claimed method of using resorbable polymer coated particles together with a calcium sulfate matrix to produce a

heterogeneous solid composition that resorbs at a controlled rate in a recipient site for stimulating bone growth.

Therefore, Applicants maintain that the claimed invention defined by Claims 36 and 38-40 are unobvious in view of the prior art.

Accordingly, Applicant respectfully requests withdrawal of the rejection of Claims 1-5, 18, 19, 33-36 and 38-40 based upon 35 U.S.C. §103(a).

It is respectfully submitted that Claims 1-5, 7-19, 21-35, 36-41 and 42-71 the pending claims, are now in condition for allowance and such action is respectfully requested. Applicant's Agent respectfully requests direct telephone communication from the Examiner with a view toward any further action deemed necessary to place the application in final condition for allowance.

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Date of Signature

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